CLAIMS

WHAT IS CLAIMED IS:

1. A method of modulating calvarial osteoblast differentiation and mineralization, said method comprising:

altering expression or activity of Nell-1, wherein increased expression or activity of Nell-1 increases osteoblast differentiation or mineralization and decreased expression or activity of Nell-decreases osteoblast differentiation or mineralization.

2. The method of claim 1, wherein Nell-1 expression or activity is inhibited is by a method selected from the group consisting of an anti-Nell-1 antisense molecule, a Nell-1 specific riibozyme, a Nell-1 specific catalytic DNA, a Nell-1 specific RNAi, anti-Nell-1 intrabodies, and gene therapy approaches that knock out Nell-1 in particular target cells and/or tissues.

3. The method of claim 1, wherein Nell-1 expression or activity is increased by a method selected from the group consisting of transfecting a cell with an exogenous nucleic acid expressing Nell-1, and transfecting a cell with a Nell-1 protein.

4. The method of claim 2, wherein said Nell-1 expression or activity is inhibited in a mammal experiencing abnormal cranial suture development.

5. The method of claim 4, wherein said abnormal cranial suture development comprises Craniosynostosis (CS).

6. A method of facilitating latent TGF-β1 activation in a mammal, said method comprising administering exogenous Nell-1 to said mammal, or increasing expression activity of endogenous Nell-1 in said mammal.

7. A method of activating or sequestering a member of the TGF-β superfamily in a mammal, said method comprising administering exogenous Nell-1 to said mammal, or increasing expression activity of endogenous Nell-1 in said mammal.

8. A method of screening for an agent that modulates osteoblast differentiation, said method comprising:

contacting a test cell containing a *NELL-1* gene with a test agent; and

detecting a change in the expression level of a *NELL-1* gene or the activity of Nell-1 in said test cell as compared to the expression of the *NELL-1* gene or the activity of Nell-1 in a control cell where a difference in the expression level of *NELL-1* or the activity of Nell-1 in the test cell and the control cell indicates that said agent modulates bone mineralization.

9. The method of claim 8, wherein said control is a negative control cell contacted with said test agent at a lower concentration than said test cell.

10. The method of claim 9, wherein said lower concentration is the absence of said test agent.

11. The method of claim 8, wherein said control is a positive control cell contacted with said test agent at a higher concentration than said test cell.

12. The method of claim 8, further comprising recording test agents that alter expression of the NELL-1 nucleic acid or the NELL-1 protein in a database of modulators of *NELL-1* activity or in a database of modulators of bone mineralization.

13. The method of claim 8, wherein the expression level of nell-1 is detected by measuring the level of *NELL-1* mRNA in said cell.

14. The method of claim 13, wherein said level of *NELL-1* mRNA is measured by hybridizing said mRNA to a probe that specifically hybridizes to a *NELL-1* nucleic acid.

15. The method of claim 14, wherein said hybridizing is according to a method selected from the group consisting of a Northern blot, a Southern blot using DNA derived from the nell-1 RNA, an array hybridization, an affinity chromatography, and an *in situ* hybridization.

16. The method of claim 15, wherein said probe is a member of a plurality of probes that forms an array of probes.

17. The method of claim 13, wherein said level of *NELL-1* mRNA is measured using a nucleic acid amplification reaction.

18. The method of claim 8, wherein said level of *NELL-1* is detected by determining the expression level of a NELL-1 protein in said biological sample.

19. The method of claim 18, wherein said detecting is via a method selected from the group consisting of capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, and immunohistochemistry.

20. The method of claim 8, wherein said cell is cultured *ex vivo*.

21. The method of claim 8, wherein said test agent is not an antibody.

22. The method of claim 8, wherein said test agent is not a protein.

23. A method of altering Nell-1 expression in a mammalian cell, said method comprising altering the expression or activity of *Msx2* and/or *Cbfa1*.

24. The method of claim 23, comprising upregulating *Cbfa1* expression or activity to upregulate Nell-1 expression or activity.

25. The method of claim 23, comprising uupregulating *Msx2* expression or activity to downregulate Nell-1 expression or activity.

26. A method of screening for an agent that modulates Nell-1 expression or activity, said method comprising:

contacting a test cell containing a *Cbfa1* and/or an *Msx2* gene with a test agent; and

detecting a change in the expression level of an *Cbfa1* and/or an *Msx2*gene or the activity of Cbfa1 and/or an Msx2 in said test cell as compared to the expression of the *Cbfa1* and/or an *Msx2* gene or the activity of Cbfa1 and/or an Msx2 in a control cell where a difference in the expression level of *Cbfa1* and/or an *Msx2*or the activity of Cbfa1 and/or an Msx2 in the test cell and the control cell indicates that said agent modulates Nell-1 expression or activity.

27. The method of claim 26, wherein said control is a negative control cell contacted with said test agent at a lower concentration than said test cell.

28. The method of claim 27, wherein said lower concentration is the absence of said test agent.

29. The method of claim 26, wherein said control is a positive control cell contacted with said test agent at a higher concentration than said test cell.

30. The method of claim 26, further comprising recording test agents that alter expression of *Cbfa1* and/or an *Msx2* gene or the activity of Cbfa1 and/or an Msx2 in a database of modulators of *NELL-1* activity or in a database of modulators of bone mineralization.

31. The method of claim 26, wherein the expression level of nell-1 is detected by measuring the level of *Cbfa1* and/or an *Msx2* mRNA in said cell.

32. The method of claim 31, wherein said level of *Cbfa1* and/or an *Msx2* mRNA is measured by hybridizing said mRNA to a probe that specifically hybridizes to a *Cbfa1* and/or an *Msx2* nucleic acid.

33. The method of claim 32, wherein said hybridizing is according to a method selected from the group consisting of a Northern blot, a Southern blot using DNA derived from the *Cbfa1* and/or *Msx2* RNA, an array hybridization, an affinity chromatography, and an *in situ* hybridization.

34. The method of claim 33, wherein said probe is a member of a plurality of probes that forms an array of probes.

35. The method of claim 31, wherein said level of *Cbfa1* and/or *Msx2* mRNA is measured using a nucleic acid amplification reaction.

36. The method of claim 26, wherein said level of *Cbfa1* and/or *Msx2* is detected by determining the expression level of a *Cbfa1* and/or *Msx2* protein in said biological sample.

37. The method of claim 36, wherein said detecting is via a method selected from the group consisting of capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, and immunohistochemistry.

38. The method of claim 26, wherein said cell is cultured *ex vivo*.

39. The method of claim 26, wherein said test agent is not an antibody.

40. The method of claim 26, wherein said test agent is not a protein.

41. A pharmaceutical formulation, said formulation comprising :

one or more active agents selected from the group consisting of a nucleic acid encoding a Nell-1 protein, a Nell-1 protein, and an agent that alters expression or activity of a Nell-1 protein; and

a pharmaceutically acceptable excipient.